

09/865,321

CASE D0028 NP

In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application. Please amend claims 70, 74, 78, 95, 96 and 114 as follows. Please add new claims 116-126 as follows.

Listing of Claims:

1 to 66. (Cancelled)

67. (Previously Presented) A CTLA4 mutant molecule which binds CD80 and/or CD86 comprising an extracellular domain of CTLA4 as shown in SEQ ID NO:8 beginning with alanine at position 26 or methionine at position 27 and ending with aspartic acid at position 150, or a portion thereof, wherein in the extracellular domain or portion thereof an alanine at position 55 is substituted with a tyrosine, and a leucine at position 130 is substituted with a glutamic acid.
68. (Previously Presented) A CTLA4 mutant molecule comprising:
- (a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of SEQ ID NO:4, or
 - (b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of SEQ ID NO:4.
69. (Previously Presented) A CTLA4 mutant molecule comprising:
- (a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of SEQ ID NO:4 or a portion thereof that binds CD80 and/or CD86, or
 - (b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of SEQ ID NO:4 or a portion thereof that binds CD80 and/or CD86.

09/865,321

CASE D0028 NP

70. (Currently Amended) The CTLA4 mutant molecule of claim 67, 68, or 69 further comprising an amino acid sequence which alters the solubility or affinity of the soluble CTLA4 mutant molecule.
71. (Previously Presented) The CTLA4 mutant molecule of claim 70, wherein the amino acid sequence which alters the solubility or affinity comprises an immunoglobulin.
72. (Previously Presented) The CTLA4 mutant molecule of claim 71, wherein the immunoglobulin is an immunoglobulin constant region or portion thereof.
73. (Previously Presented) The CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is mutated to reduce effector function.
74. (Currently Amended) The CTLA4 mutant molecule of claim 72 or 73, wherein the immunoglobulin constant region comprises a hinge, CH2 and CH3 regions of an immunoglobulin molecule.
75. (Previously Presented) The CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is a human or monkey immunoglobulin constant region.
76. (Previously Presented) A CTLA4 mutant molecule comprising:
- (a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO:4, or
 - (b) an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO:4.
77. (Previously Presented) A CTLA4 mutant molecule consisting of:
- (a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO:4, or

09/865,321

CASE D0028 NP

- (b) an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO:4.
78. (Currently Amended) The CTLA4 mutant molecule of claim 67, 68, 69, or 76 further comprising an amino acid sequence which permits secretion of the soluble CTLA4 mutant molecule.
79. (Previously Presented) The CTLA4 mutant molecule of claim 78, wherein the amino acid sequence which permits secretion comprises an oncostatin M signal peptide.
80. (Previously Presented) A CTLA4 mutant molecule comprising an amino acid sequence beginning with methionine at position 1 and ending with lysine at position 383 of SEQ ID NO:4.
81. (Withdrawn) A nucleic acid molecule encoding the soluble CTLA4 mutant molecule of claim 67, 68, 69, 76, 77 or 80.
82. (Withdrawn) The nucleic acid molecule of claim 81 comprising:
- (a) the nucleic acid molecule beginning with adenine at position 79 and ending with thymine at position 450 of SEQ ID NO:3, or
 - (b) the nucleic acid molecule beginning with guanine at position 76 and ending with thymine at position 450 of SEQ ID NO:3.
83. (Withdrawn) The nucleic acid molecule of claim 81 comprising:
- (a) the nucleic acid molecule beginning with adenine at position 79 and ending with adenine at position 1149 of SEQ ID NO.: 3, or
 - (b) the nucleic acid molecule beginning with guanine at position 76 and ending with adenine at position 1149 of SEQ ID NO:3.

09/865,321

CASE D0028 NP

84. (Withdrawn) The nucleic acid molecule of claim 81 comprising the nucleic acid molecule beginning with adenine at position 1 and ending with adenine at position 1149 of SEQ ID NO.: 3.
85. (Withdrawn) A DNA molecule encoding a soluble CTLA4 mutant molecule, wherein the DNA molecule is deposited as ATCC No. PTA-2104.
86. (Previously Presented) A CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104.
87. (Withdrawn) A vector comprising the nucleic acid molecule of claim 81.
88. (Withdrawn) A vector comprising the DNA molecule of claim 85.
89. (Withdrawn) A vector encoding a soluble CTLA4 mutant molecule and deposited with the ATCC as ATCC No. PTA-2104.
90. (Withdrawn) A host cell having the vector of claim 87, 88, or 89.
91. (Withdrawn) The host cell of claim 90 which is a bacterial or eukaryotic cell.
92. (Withdrawn) The host cell of claim 91, wherein the eukaryotic cell is a COS cell or a Chinese Hamster Ovary (CHO) cell.
93. (Withdrawn) A method for producing a soluble CTLA4 mutant molecule comprising growing the host cell of claim 90 so as to produce the soluble CTLA4 mutant molecule in the host cell, and recovering the molecule so produced.
94. (Cancelled)

09/865,321

CASE D0028 NP

95. (Currently Amended) A CTLA4 mutant molecule comprising the entire extracellular domain of the ~~soluble~~ CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104.
96. (Currently Amended) A pharmaceutical composition comprising a CTLA4 mutant molecule of claim 67, 68, 69, 74, 76, 77, 86, or 95 and a pharmaceutically acceptable carrier.
- 97 to 103. (Cancelled)
104. (Previously Presented) The CTLA4 mutant molecule of claim 71, wherein the immunoglobulin comprises a hinge and any or all of the cysteine residues within the hinge are substituted with serine.
105. (Previously Presented) The CTLA4 mutant molecule of claim 104, wherein a cysteine at position +156 is substituted with a serine, a cysteine at position +162 is substituted with a serine, and a cysteine at position +165 is substituted with a serine, as shown in SEQ ID NO:4.
106. (Previously Presented) The CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is mutated to include a cysteine at position +156 substituted with a serine, a cysteine at position +162 substituted with a serine, a cysteine at position +165 substituted with a serine, and a proline at position +174 substituted with serine, as shown in SEQ ID NO:4.
107. (Previously Presented) The CTLA4 mutant molecule of claim 71, wherein the immunoglobulin comprises an amino acid sequence which begins with glutamic acid at position +152 and ends with lysine at position +383, as shown in SEQ ID NO:4.
108. (Previously Presented) The CTLA4 mutant molecule of claims 67, 68, or 69, further comprising a junction amino acid residue and an immunoglobulin, where the junction

09/865,321

CASE D0028 NP

amino acid residue is located between the amino acid sequence which ends with aspartic acid at position +150 and the immunoglobulin.

109. (Previously Presented) The CTLA4 mutant molecule of claim 108, wherein the junction amino acid residue is glutamine.
- 110 to 112. (Cancelled)
113. (Previously Presented) The CTLA4 mutant molecule of claims 67, 68, 69, 76 or 77, that has a slower dissociation rate from binding CD86 than wild type CTLA4.
114. (Currently Amended) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, that is soluble.
115. (Cancelled)
116. (New) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, that is substantially pure.
117. (New) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, wherein the CTLA4 mutant molecule is a dimer.
118. (New) The CTLA4 mutant molecule of claims 67, 68, 69, 74, 76, 77, 86, or 95, wherein the CTLA4 mutant molecule has a molecular mass of about 100 kilodaltons.
119. (New) The CTLA4 mutant molecule of claim 118, wherein the molecular mass is assessed by SDS-PAGE under non-reducing conditions.
120. (New) The CTLA4 mutant molecule of claim 73, wherein the immunoglobulin constant region comprises a hinge, CH2 and CH3 regions of an immunoglobulin molecule.

09/865,321

CASE D0028 NP

121. (New) A pharmaceutical composition comprising a CTLA4 mutant molecule of claim 120 and a pharmaceutically acceptable carrier.
122. (New) The CTLA4 mutant molecule of 120, that is soluble.
123. (New) The CTLA4 mutant molecule of claim 120, that is substantially pure.
124. (New) The CTLA4 mutant molecule of claim 120, wherein the CTLA4 mutant molecule is a dimer.
125. (New) The CTLA4 mutant molecule of claim 120, wherein the CTLA4 mutant molecule has a molecular mass of about 100 kilodaltons.
126. (New) The CTLA4 mutant molecule of claim 125, wherein the molecular mass is assessed by SDS-PAGE under non-reducing conditions.